References

1. MILLER MJ, MAYNARD GR: Creeping eruption treated by thiabendazole; case. *Can Med Assoc J* 97: MJ, Cutan. 860, 1967
2. STONE OJ, NEWELL GB, MULLINS MJ, Cutaneous strongyloidiasis: larva currens. *Arch Dermatol* 106: 734, 1972
3. Personal correspondence

Multiple sclerosis and other demyelinating diseases

To the Editor:

Multiple sclerosis has been defined as a chronic progressive disease of the central nervous system, or rather a series of syndromes based on several as-yet-undetermined causative factors.[1] The etiologic factor or factors are unknown, but Harrison[2] has emphasized its relationship to other demyelinating processes. The pathological change underlying multiple sclerosis is presumed to be demyelination in scattered areas of the brain and spinal cord in plaques of varying size. There is associated edema of the axons and, with progression, degeneration and loss of function. Vitamins B_1 and B_{12} are both essential components of myelin.[4,5] Because demyelination of long nerve axons in the spinal cord is characteristic of severe vitamin B_{12} deficiency and because this vitamin arrests demyelination in combined system disease, it has been used in the treatment of multiple sclerosis with varying results.[1-3,6-8]

On the theory that demyelination results from the lack of vitamin B_1 and some factor or factors in liver extract, a therapeutic trial was initiated by the undersigned in 1943. The purpose of this letter is to report the results of that trial.

Materials and methods: Patients were selected on the basis of a history of neurologic deficits suggestive of multiple sclerosis which had been confirmed by neurologic investigation and, in most patients, by a second opinion. The presence of paralysis was felt to be a contraindication to this type of therapy. Fourteen patients were followed up for periods varying from several months to 29 years (Table I).

Routine therapy consisted of in-

Table I
Fourteen patients with multiple sclerosis treated with thiamine hydrochloride and liver extract

Case	Age at onset	Age at 1st treatment	Treatment	Duration of treatment	Current clinical status	Patient's estimate of improvement
1	22	26	Irregular*	1943-1972	Clinically well	95%
2	38 mild 43 severe	43	Irregular	1947-1972	Clinically well	85%
3	26	57	Regular†	1970-1972	Clinically improved	80%
4	25	28	Regular	1971-1972	Clinically well	98%
5	20	41	Regular	1971-1972	Clinically improved	75%
6	26	31	Regular	July-Dec. 1972	Clinically well	95%
7	27	30	Irregular	1971-1972	Improved	50%
8	13 mild 40 severe	49	Regular	1971-1972	Greatly improved	95%
9	37	39	Regular	1971-1972	Improving	50%
10	17	24	Irregular	1964-1972	Improved	80%
11	17	19	Irregular	1962-1964 1967, Mar. 1972	Clinically well	95%
12	48	55	Irregular	1969-1972	Improved	40%
13	35	38	Regular	July-Dec. 1972	Improved	75%
14	26	28	Regular	Jan.-Feb. 1973	Improved	50%

*Irregular: patient receives regular treatment for a period and then does not return for supervision, generally because he or she feels well.
†Regular: patient cooperates in returning for routine therapy.

travenous thiamine hydrochloride, 150 mg., plus intramuscular injections of liver extract*, 20 μg. (1 ml.), every seven to 10 days for a series of 10 treatments. The patient was then re-evaluated neurologically. Further treatment was recommended depending on the status of the neurologic deficit and the response.

Results and conclusions: The results in the treated patients are summarized in Table I. No patient had progression of the disease while on treatment. When symptoms recurred on cessation of treatment, they were controlled by resumption of therapy.

When vitamins B_1 and B_{12} were given simultaneously to one patient (case 1) on two occasions (owing to sensitization to liver extract) the patient experienced progression of her deficit. When liver extract and vitamin B_1 therapy was resumed (following desensitization) she improved.

A trial of thiamine hydrochloride, 100 mg. daily by mouth, with regular liver extract therapy (case 4) led to return of symptoms. When routine therapy was again resumed all symptoms cleared. It would appear that some persons may not absorb vitamin B_1 through the gastrointestinal tract.

Patients treated in the early stages of the disease responded well and within a time span appropriate to the presumed underlying pathology of demyelination. Patients in whom the disease was more advanced responded more slowly. Early treatment of the disease or its recurrent symptoms seemed to be more important than the age of the patient. For example, one patient (case 1), now aged 55, still returns for treatment when she considers it necessary because of a lowered sense of well-being, increased fatigue, and a tingling sensation in her hands and feet. Thirty-three years after the onset of her illness and after bed confinement for two years, she is active, does her housework, walks out alone without a cane and enjoys an active social life.

The exact stage of pathological change in any patient cannot be determined.[7] It is logical to assume, however, that the axis cylinders had not been destroyed in any of the patients in this study, even in case 3, a 59-year-old man who refused to accept active therapy until his disease, after many years, had induced almost total incapacity, including poor writing ability and spastic and ataxic gait with dragging of the left foot. His clinical improvement continues and we must assume that remyelination is taking place. At present, this man uses a cane only on the street, can step up with either foot and even uses a ladder. His manual dexterity is good and he writes well.

My experience, like that of Evers,[9] suggests that early treatment is important in producing symptomatic relief and a state of well-being. In case 2, the patient was treated within six months of the onset of severe symptoms at age 43, made a rapid recovery and gave birth to a normal child two years later. On several occasions, because of irregular therapy, her symptoms recurred, but when treatment was resumed she improved rapidly. Now, at the age of 69, she is active and able to do her housework. In case 4, treatment was instituted within three years of the onset of the disease. The patient cooperated completely and therapy was continued without interruption. After nine months he stated that he felt perfectly well.

The effects of cessation and resumption of therapy are most clearly demonstrated in case 11. Following initial treatment from 1962 to 1964, her condition was improved and treatment was discontinued. In 1967, because of recurrence of symptoms, therapy was resumed on an irregular basis with subsequent improvement. In February 1971 the patient returned with symptoms of fatigue, inability to work, loss of balance and staggering gait. She was not able to return for therapy until March 1972, at which time her neurologic condition had worsened. She had visual and auditory difficulty, scanning speech and poor writing ability, unsteady gait and poor sense of balance. Routine therapy was recommenced and by June 20 of the same year she was able to return to work as a typist and stated that she felt perfectly well.

The protracted and capricious natural history of multiple sclerosis precludes dogmatic statements regarding the effect of a new therapeutic modality. Furthermore, the exact diagnostic criteria of multiple sclerosis are uncertain, leading to a frequent diagnosis by exclusion appropriate to the uncertainty regarding etiology and pathogenesis. However, with regard to the therapy presented here, patients with two other types of demyelinating diseases have been successfully treated. One of these, a patient with advanced bulbar palsy, is now almost completely asymptomatic. The other, a patient with subacute combined sclerosis who was totally incapacitated, became neurologically entirely negative. My experience suggests that some factor or factors in liver extract, associated with vitamin B_1, can induce remyelination in patients suffering from multiple sclerosis and probably in other cases of demyelinating diseases. It is suggested that this clinical finding should now be subjected to detailed laboratory studies in order to enlarge its use or to circumscribe its limitations.

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*Therapy was begun with Lederle's liver extract, but production ceased in the spring of 1972. Connaught Laboratory liver extract was used for a period of nine months. Lilly's liver extract is now used.

References

1. Wechsler IS: *Clinical neurology*, ninth ed. Philadelphia, WB Saunders, 1963
2. Harrison TR: *Principles of Internal Medicine*, sixth ed, vol 2. Toronto, McGraw-Hill, 1970, pp 1080-2016
3. Lehrer GM: Etiology, diagnosis and treatment of multiple sclerosis. *Mod Treat* 7: 1970
4. Cures for multiple sclerosis. *Br Med J* I: 59, 1970
5. Norman CS: Vitamin B_{12} plasma clearance in multiple sclerosis. *Ir J Med Sci 6:* 333, 1966
6. Merritt HN: *Textbook of Neurology*, fourth ed. Philadelphia, Lea and Febiger, 1967, pp 704-727
7. Namerow NS, Thompson LR: Plaques, symptoms, and the remitting course of multiple sclerosis. *Neurology (Minneap)* 19: 765, 1969
8. Simpson CA, Newell DJ, Miller H: The treatment of multiple sclerosis with massive doses of hydroxycobalamin. *Neurology* 15: 599, 1965
9. Evers J: Dietetic therapy of multiple sclerosis *Med Welt* 20: 1700, 1969